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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/060,697	01/30/2002	Donald W. Petersen	06317-038003	8553

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BOSTON, MA 02110

EXAMINER

WITZ, JEAN C

ART UNIT	PAPER NUMBER
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1651

DATE MAILED: 10/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No. 10/060,697	Applicant(s) PETERSEN, DONALD W.	
	Examiner Jean C. Witz	Art Unit 1651	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.
Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

- a) ☒ The period for reply expires 6 months from the mailing date of the final rejection.
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on 02 October 2003. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
(b) ☐ they raise the issue of new matter (see Note below);
(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.
4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attached.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

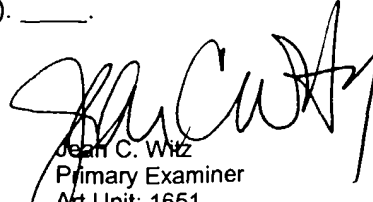
Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: 16-30.

Claim(s) withdrawn from consideration: _____.

8. ☐ The proposed drawing correction filed on _____ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____.
10. ☐ Other: _____


Jean C. Witz
Primary Examiner
Art Unit: 1651

DETAILED ACTION

Response to Arguments

Applicant's arguments filed August 26, 2003 have been fully considered but they are not persuasive for the reasons set forth below.

Applicant has argued that there is no motivation to combine the references in the rejection of record. Applicant states that "the fact that the components could be removed from the other compositions and combined to obtain the claimed compositions is not a sufficient basis for obviousness." However, Applicant does not address the fact that each individual ingredient found in each of the references is taught to be added for a specific effect. The ingredients are separate and in fact, separable, as the reference teach various combinations of the ingredients.

Applicant appears to continue to assert that Wironen teaches away from the disclosure of O'Leary by stating "a person skilled in the art reading Wironen would be discouraged from looking to O'Leary. Wironen expressly characterizes O'Leary as being "a non-cross-linkable composition" (page 3, lines 22-23), which contrasts with Wironen's explicit requirement of a composition being "cross-linkable" (page 5, line 25). Thus, taken as a whole, a person skilled in the art reading Wironen would not be motivated to look to O'Leary, let alone combine the teachings of O'Leary with the teachings of Wironen." Applicant had previously asserted that Wironen taught away by reference to a commercially available product covered by the O'Leary patent that uses glycerol as the carrier, but Applicant completely ignored the teaching of O'Leary that does not require the presence of glycerol and does allow the inclusion of a cross-linkable

component such as collagen or gelatin. See O'Leary, claim 11. Therefore, Wironen only teaches away from a specific embodiment of O'Leary; however, as stated in the previous office action, the teaching of a U.S. Patent is not limited to its preferred embodiments. Therefore, Applicant's arguments to that end are not found to be persuasive.

Applicant further argues that

"With regard to combining Wironen with Yim, Wironen discloses using a gelatin as a carrier that has the ability to thermally cross-link (page 5, line 25). But neither Wironen nor Yim discloses or suggests that calcium sulfate is a carrier that has the ability to thermally cross-link. Without such a teaching, there is no suggestion or motivation in Wironen or Yim to combine calcium sulfate with the cancellous bone of Wironen. Thus, there a person of ordinary skill in the art would not have been motivated by the teachings of Wironen or Yim to form a composition of claim 16 or claim 27. Because O'Leary teaches compositions including demineralized bone, and does not teach or suggest compositions that include calcium sulfate or cross-linking, a person of ordinary skill would not have been motivated to combine any teaching of O'Leary with the teachings of Wironen or Yim. Thus, in the absence of hindsight, there is no motivation to combine the teachings of O'Leary, Wironen and Yim."

Applicant's arguments that neither Wironen or Yim suggests that calcium sulfate is a crosslinking agent is again not germane to the rejection of record. In the previous office action, the Examiner pointed out that the disclosure of WO 9840113 is also drawn to a bone paste for the repair of bone defects. The disclosed paste contains demineralized bone matrix, an inorganic component such as ceramics hydroxyapaptite and calcined bone, or bone morphogenic proteins or other growth factors and mixtures thereof. Other ingredients that may be present in the paste include wetting agents and carboxymethylcellulose (see pages 5-6). At page 13, the reference states that the composition "may act as a carrier for cortical, cancellous or cortical and cancellous bone

chips. Such compositions are useful for filling larger bone voids. In addition, when these bone chips are not demineralized, they provide an added spectrum of biological properties not exhibited by the gelatin alone or the gelatin plus the osteogenic components (i-iv).” Therefore, the disclosure of Wironen was specifically included in the rejection to teach that one of ordinary skill in the art would be aware that there is a motivation to include cancellous bone into a bone repair composition for the reasons set forth above. Applicant again appears to be arguing that the disclosure of Wironen be interpreted to mean that cancellous bone can only be included in the composition of Wironen or that if cancellous bone is included in the composition of O’Leary, so must the gelatin; however, that interpretation is too limited since the benefits that the cancellous bone brings to the composition of Wironen would be expected by one of ordinary skill in the art to accrue to other bone repair compositions and as stated above, O’Leary includes gelatin in embodiments. O’Leary, Yim and even Wironen himself provide disclosures such as found in virtually every patent document as exemplified at page 6 of the Wironen document which states that “Other factors [followed by a list of substances] . . . or combinations thereof or any other material found to add to the desirable properties of the essential composition of this invention may be included.” Statements of this type recognize that other ingredients have known benefits and may be added to disclosed compositions for their contribution to the composition in question. Therefore, there is a motivation to include the cancellous bone described by Wironen into the O’Leary composition.

Applicant further argues that there is no motivation to combine the calcium sulfate of Yim into the composition of O'Leary. Applicant asserts that the "reasons for adding calcium sulfate are either inconsistent with the type of compositions that O'Leary intended to form or have already been addressed by O'Leary." Applicant points to improving retention and reducing setup time "suggest that the composition should be relatively viscous, but then points to the embodiments of O'Leary where "the compositions are intended to be 'runny'." Applicant then asserts that where the embodiments are intended to be "like a putty", the thickener fulfills this purpose; therefore, the addition of the calcium sulfate in "unnecessarily redundant, and as a result, there is no motivation to form Applicant's claimed composition."

This argument fails to take into consideration that O'Leary envisions a range of consistencies of the composition and defines "the term 'flowable' as used herein applies to compositions whose consistencies range from those which can be described as shape-sustaining but readily deformable, e.g., those which behave like putty, to those which are runny. Specific forms of flowable bone powder compositions include cakes, pastes, creams and fillers." O'Leary et al. state at col. 1, lines 36-43 that "[I]t is a particular object of the invention to provide a composition of liquid or pastelike consistency comprising demineralized osteogenic bone powder and a biocompatible liquid synthetic organic material as a carrier for the bone powder with or without such optional ingredients as thixotropic agents, medicaments, and the like, and to apply the composition at a bone defect site to induce new bone ingrowth at the site."

Therefore, the goal of the invention is to provide a composition that is a carrier for the demineralized bone powder as well as other optional ingredients. O'Leary et al. disclose at col. 2, line 53 to col. 3, line 13, that "[a]ny of a variety of substances can be introduced into the bone particles" and includes a non-limiting list which includes inorganic elements, parenchymal cells, growth factors, bone morphogenic proteins, and mesenchymal elements. " (emphasis added.) Calcium sulfate would be considered by one of ordinary skill in the art to be such an "inorganic element".

Yim specifically teaches that "[t]o reduce the preparation time and improve the above formulation's handling characteristics, [Patentees] have surprisingly found that it is desirable to add a calcium sulfate hemihydrate-containing substance (CSHS). The CSHS is preferably either pure calcium sulfate hemihydrate, also known as Plaster of Paris (POP), or a mixture of POP and hydroxyapatite (POP:HA). Adding a CSHS reduces setup time and provides improved moldability and consistency of the resulting formulation." The "above formulation" includes osteogenic proteins and a suitable "protein-sequestering agent", disclosed at col. 7, lines 25-34, as cellulosic materials such as alkylcelluloses (including hydroxyalkylcelluloses), such as methylcellulose, ethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropyl-methylcellulose, and carboxymethylcellulose. It is noted that Yim already includes the thickener of O'Leary yet finds that the addition of calcium sulfate improves the composition for certain applications . As a result, one of ordinary skill in the art would expect the composition of O'Leary would similarly be improved for certain applications by the inclusion of calcium sulfate, as one of ordinary skill in the art would also expect

that the composition of O'Leary would be improved for certain applications by the inclusion of the cancellous bone disclosed by Wironen. There is no suggestion in the O'Leary reference that it will become inoperative with the inclusion of other ingredients and in fact, as indicated above, suggests that other ingredients may be included.

Therefore, the references, as a whole, certainly provide motivation to add both the calcium sulfate of Yim and the cancellous bone of Wironen to the composition of O'Leary with the expected known and disclosed benefit that both components will add to the composition of O'Leary. Both O'Leary et al. and Yim et al. have the same object in creating a malleable, workable bone growth promoting composition. One of ordinary skill in the art when reviewing the disclosure of Yim would have been motivated to include a calcium sulfate component into the composition of O'Leary et al. with the expected benefit disclosed by Yim et al., i.e. that a calcium sulfate component would add improved handling, moldability and consistency to the formulation of O'Leary as well as reducing the set up time. The compositions of Yim and O'Leary are so sufficiently similar that one of ordinary skill in the art at the time the invention was made would be aware of the properties of the calcium sulfate hemihydrate would not impair or otherwise negatively affect the components of the O'Leary composition. Both compositions contain components that provide either directly or indirectly osteogenic proteins, and both compositions contain a cellulosic material which is being used for the same purpose, i.e. to impart viscosity and suspension properties to the respective compositions. The general amounts of both the demineralized bone matrix and the cellulose material are taught by the references. The optimization of the amount of

calcium sulfate and mixing solution to be further included is deemed well within the skill of the practitioner at the time the invention was made as it is clear that the amount of calcium sulfate is directly related to desired rate of set up of the composition, i.e. the more calcium sulfate used, the faster the composition will set up and harden. Further, it is clear that the amount of mixing solution is inversely related to the desired set up time and directly proportional to the ultimate consistency of the composition, i.e. the more mixing solution used, the more dilute the calcium sulfate and the slower the set up time but the more liquid the composition will become.

Finally, the claims recite the further inclusion of cancellous bone. Both patents teach that other conventional components included in bone growth promoting compositions may be included in the disclosed compositions. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include cancellous bone chips into the composition of O'Leary et al. for the benefit described in the disclosure of WO 9840113, i.e. they fill larger bone voids and provide an added spectrum of biological properties to the composition.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jean C. Witz whose telephone number is (703) 308-3073. The examiner can normally be reached on 6:30 a.m. to 4:00 p.m. M-Th and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (703) 308-4743. The fax phone numbers for the organization where this application or proceeding is assigned are (703)

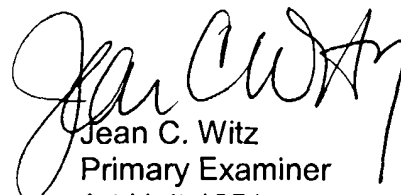
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872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.


Jean C. Witz
Primary Examiner
Art Unit 1651

October 24, 2003